

### Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

This submission is accompanied by a Request for Continued Examination, a petition for extension of time, and an information disclosure statement. All fees should be withdrawn from Deposit Account 14-1138.

Claim 1 has been amended to recite higher stringency requirements (i.e., structural requirements of the claimed DNA molecule based on hybridization capability) as well the functional requirements of the encoded single-strand binding protein subunit ("binds to single-stranded DNA"). A form of the latter limitation also appears in original claim 6. Claims 8 and 9 have been cancelled.

Claims 1, 2, 5-7, and 10-17 are pending. Claims 15-17 stand allowed.

The rejection of claims 1, 2, and 5-14 under 35 U.S.C. §112 (first paragraph) as lacking written descriptive support is respectfully traversed.

The PTO has asserted at page 4 of the outstanding office action that the "function" of the claimed single-strand binding protein remains in question. Applicants respectfully disagree.

Claim 1 presently recites that "isolated single-strand binding protein binds to single-stranded DNA." Persons of skill in the art would appreciate that this is precisely the function attributed to single-strand binding proteins that cooperate with polymerase<sup>5</sup> in general, including polymerase III enzyme complexes. Indeed, the single-strand binding protein of *E. coli* was previously shown to bind cooperatively to single-stranded DNA and destabilize helical duplexes, causing a lowering of the melting temperature (*see* Kunkel et al., "Single-strand Binding Protein Enhances Fidelity of FNA Synthesis *in vitro*," *Proc. Natl. Acad. Sci. USA* 76(12):6331-6335 (1979) ("Kunkel") at p. 6331 (copy attached hereto as **Exhibit 1**)). Kunkel even reports that the *E. coli* single-strand binding protein, when used with the *E. coli* Pol III enzyme complex and DNA polymerases of *divergent sources*, was capable of increasing fidelity by as much as 10-fold. Kunkel at abstract.

Use of single-strand binding proteins of the present invention in combination with a Pol III-type enzyme is clearly contemplated (*see* page 44, lines 17-19, and page 45, lines 2-4 ("The reaction is incubated at elevated temperature ... and could include other proteins to enhance activity such as a single strand DNA binding protein.")). This

combination would be expected to function in a similar manner to other prior art single-strand binding proteins.

Given the shared function among single-stranded binding proteins, persons of skill in the art would have expected a shared structure/function relationship to exist. In fact, De Vries et al. reported as early as 1994 that the N-terminal amino acid sequences of single-strand binding proteins are highly conserved within the first two-thirds of the protein sequence and highly divergent within the C-terminal third. De Vries et al., "The Single-stranded-DNA-binding Proteins (SSB) of *Proteus mirabilis* and *Serratia marcescens*," *Eur. J. Biochem.* 224:613-622 (1994) at abstract and Fig. 2 (copy attached as **Exhibit 2**). Thus, persons of skill in the art would have expected both structural and functional conservation among single-strand binding proteins.

That the isolated single-strand binding protein is structurally related to other single-strand binding proteins is evident from the comparison of the *Thermus thermophilus* single-strand binding protein of SEQ ID NO: 172 to the *B. stearothermophilus* single-strand binding protein of SEQ ID NO: 176 (see page 61, line 32, to page 62, line 2). These two species show about 23 percent identity over their length.

From the foregoing, persons of skill in the art would have expected members of the claimed genus of single-stranded binding proteins to possess both similar function and structure. Indeed, even higher similarity among single-strand binding proteins would be expected among more closely related bacteria, and that is precisely what applicants demonstrated in the previous response (see Exhibits 1-3 attached to the August 22, 2006, amendment). Thus, given applicants prior demonstration of structural similarity among homologous single-strand binding proteins subunits of *Bacillus*, applicants respectfully submit that the genus of isolated DNA being claimed is adequately represented by the species of SEQ ID NO: 176.

In view of all of the foregoing, applicants submit that the rejection of claims 1, 2, and 5-14 is improper and should be withdrawn.

The rejection of claims 1, 2, and 5-14 under 35 U.S.C. §112 (first paragraph) for lack of enablement is respectfully traversed.

It is the position of the PTO that the specification does not provide sufficient guidance for making and using other single-strand binding proteins within the scope of the claims. Applicants respectfully disagree.

The present application provides the nucleotide sequence of *Bacillus stearothermophilus ssb* (e.g., SEQ ID NO: 175) and describes how one of ordinary skill can

isolate homologs of the disclosed sequence (*see* page 41, line 9 to page 42, line 29; Example 12), express the SSB protein encoded by such homologous *ssb* sequences (*see* Example 23, purifying *Aquifex* SSB protein), and test the encoded SSB protein for activity (*see* Examples 26 and 30, using *Aquifex* SSB protein in assay). Thus, one of ordinary skill in the art would have been fully able to make and use DNA molecules and their encoded proteins within the scope of the presently claimed invention.

Moreover, with regard to method 3 for homolog identification, described at page 42, that is precisely the approach used to identify the *ssb* homologs shown in Exhibit 1 of applicants' August 22, 2006, submission (i.e., from other *Bacillus* or *Geobacillus* organisms). For this reason, it should be apparent that the present application fully enables the production and use of other species of *Bacillus* or *Bacillus* (now *Geobacillus*) *stearothermophilus* SSB proteins.

For these reasons, applicants submit that the rejection of claims 1, 2, and 5-14 for lack of enablement is improper and should be withdrawn.

In view of all of the foregoing, applicant submits that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

Date: November 26, 2007

/Edwin V. Merkel/  
Edwin V. Merkel  
Registration No. 40,087

NIXON PEABODY LLP  
1100 Clinton Square  
Rochester, New York 14604  
Telephone: (585) 263-1128  
Facsimile: (585) 263-1600